

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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**Serial Number:** 10/671,086

**Filing Date:** 09/25/2003

**Applicant:** Alvord, et al.

**Title:** Tantalum Water Target Body for Production of  
Radioisotopes

**Docket Number:** 29363.00

**Examiner:** Daniel Lawson Greene

**Art Unit:** 3641

**Customer Number:** 22465

**Declarant:** Charles W. Alvord

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**DECLARATION OF CHARLES W. ALVORD UNDER 37 C.F.R. § 1.132**

1. I, Charles W. Alvord, declare as follows, under penalty of perjury.
2. I hold a Bachelor's of Arts in Physics from the University of California, Berkeley, awarded in 1984, a Master's of Science in Nuclear Engineering from The University of Tennessee, awarded in 2004, and I am working on my Ph.D. in Nuclear Engineering from The University of Tennessee. I have authored numerous articles, including *Computer Simulation Tools as Applied to Radioisotope Production Target Design*, J. LABEL COMP. RADIOPHARM., 2002, 45, 995-1003; *Target and Accelerator Developments at CTI*, Proceedings of the Sixteenth International Conference on the Application of Accelerators in Research and Industry, Univ. of North Texas, 2000, AIP Conf. Proc, Vol. 576, 799-803; *Computational Fluid Dynamics Study of Water Target Design and Operational Parameters*, Proceedings of the Fifteenth International Conference on the Application of Accelerators in Research and Industry, Univ. of North Texas, 1998; *Tantalum [<sup>18</sup>O] Water Target for the Production of [<sup>18</sup>F]Fluoride with High Reactivity for the Preparation of 2-Deoxy-2-[<sup>18</sup>F] Fluoro-D-Glucose*, MOL. IMAG. BIOL., 2002, 4: 65-70; among many other articles.

3. My position at CTI Cyclotron Systems, Inc. is Manager of Cyclotron Research and Development, which I have held since 2001. In this position, I manage between 8 and 14 engineers, scientists, and technicians and have the technical and engineering responsibility for the work performed in isotope target development. Before then, I was Manager of Accelerator Physics for two years and a Research and Development Engineer for nine years, both at CTI Cyclotron Systems. I have also worked as a Research Engineer at Varian Associates in Palo Alto, California for six years. I have obtained three United States patents and am named as an inventor on five pending United States patent applications.

4. I have reviewed Application Serial Number 10/671,086, filed on 09/25/2003, and titled "Tantalum Water Target Body for Production of Radioisotopes." The paragraph numbers referenced below are the paragraph numbers of the Application as filed, which are different than the paragraph numbers in the published application, Number 2005/0084055.

5. I have reviewed United States Patent Number 6,586,747, titled "Particle accelerator assembly with liquid-target holder," and issued to Erdman, et al., on July 1, 2003, and filed on June 23, 2000 (Erdman). I have reviewed the article titled "Tantalum [ $^{18}\text{O}$ ] Water Target for the Production of [ $^{18}\text{F}$ ]Fluoride with High Reactivity for the Preparation of 2-Deoxy-2-[ $^{18}\text{F}$ ] Fluoro-D-Glucose," by N. Satyamurthy, et al., and published in Molecular Imaging and Biology, Vol. 4, No. 1, at 65-70, 2002.

6. Among the optical devices with which I was familiar prior to the filing date of Application Serial Number 10/671,086, were devices of the type shown in the patent and article listed in paragraph 5 and described as prior art in Application Serial Number 10/671,086.

7. In the design and construction of a target assembly such as the ones described in Application Serial Number 10/671,086, including the prior art assemblies contained in that Application, various factors must be considered. These factors include the chemical reactions of the reagents and containers; the fluid dynamics of the reagents and coolant; the heat transfer of the reagents, the target

assembly, and the coolant; the cooling of the target assembly; and the radiation effects from the particle beam, including secondary radiation and target heating. Accordingly, one skilled in the art must be familiar with chemical reactions, fluid dynamics, heat transfer, cooling, and radiation effects. A person skilled in the art of designing and building target assemblies for producing radiopharmaceuticals is an engineer with either training or experience in chemical reactions, fluid dynamics, heat transfer, cooling, and radiation effects.

**Examiner's Statement Regarding Objection to Specification**

8. I have reviewed the U.S. Patent and Trademark Office Action, Paper Number 20050411, which contains the following statement on pages 5 and 6 with respect to the specification of Application Serial Number 10/671,086:

8. The specification is objected to under 35 U.S.C 112, first paragraph, as failing to provide an adequate written description of the invention and as failing to adequately teach how to make and/or use the invention, i.e. failing to provide and [sic] enabling disclosure.

A. Paragraph [0027] states that it is the high Reynolds number indicating turbulent flow that compensates for the low thermal conductivity of the tantalum target assembly, but paragraph [0029] contradicts this by stating it is the developed flow of the cooling water that allows for greater heat transfer, therefore the specification is insufficient and non enabling in disclosing how and in what manner the lower thermal conductivity is accounted for.

B. Paragraph [0031] states that the function of inducing fluid flow within the target chamber is accomplished by the shape of the target chamber and in another embodiment it is the size of the front window. The specification is insufficient in disclosing how and in what manner either of these will actually induce said flow.

C. The specification is insufficient in disclosing the meets and bounds of the terms "developed flow", "nearly developed flow", "fully developed flow" and "turbulent flow"

9. The statement from the Examiner quoted in Paragraph 8 is incorrect, in view of the state of the art as of the filing date of Application Serial Number 10/671,086. The Examiner's assertions are not correct, for the following reasons:

10. I have reviewed paragraphs 27 to 29 of Application Serial Number 10/671,086 in view of the Examiner's comments stated above. These paragraphs include a discussion of the theory behind the cooling channels **504, 506**. The Examiner states that the statement regarding the Reynolds number value contradicts the statement regarding developed flow. I fail to see any contradiction between these statements. Many factors contribute to heat transfer between a fluid flowing in a channel and the channel itself. It is also noted that fully turbulent flow, as characterized by Reynolds number, only develops in channels of sufficient length. Therefore, there is no contradiction between "developed flow" and "high Reynolds number." In fact, they are related concepts. A reading of Application Serial Number 10/671,086, along with the knowledge one skilled in the art would have, provides sufficient information for one skilled in the art to understand the discussion contained in Paragraph 27 relating to the flow of the cooling water through the channels **502, 504, 506, 508**.

11. I have reviewed paragraph 31 of Application Serial Number 10/671,086 in view of the Examiner's comments stated above. Paragraph 31 discusses the fluid flow in the target chamber **104'**. I have also reviewed paragraph 28 of Application Serial Number 10/671,086 in which the fluid dynamics of the target chamber **104'** are explained, including the effects due to the characteristics of the window **312** and the circular region **312** (the beam strike area). A reading of Application Serial Number 10/671,086, in particular paragraphs 28 and 31, along with the knowledge one skilled in the art would have, provides sufficient information for one skilled in the art to understand the functions enumerated in paragraph 31.

12. The terms "developed flow", "nearly developed flow", "fully developed flow" and "turbulent flow" are terms and concepts taught to engineering students in a typical fluid dynamics class. A person skilled in the art for the subject matter of Application Serial Number 10/671,086 would, as a minimum, be familiar with the terms and concepts of "developed flow", "nearly developed flow", "fully developed flow" and "turbulent flow" and would not need further explanation of such basic concepts in order to understand the invention disclosed in Application Serial Number 10/671,086.

**Examiner's Statement Regarding Rejection of Claims 7, 8, 22-27, 29-31, 33, and 34 under 35 U.S.C. § 112, first paragraph**

13. I have reviewed the U.S. Patent and Trademark Office Action, Paper Number 20050411, which contains the following statement on pages 6 and 7 with respect to the Examiners rejection of Claims 7, 8, 22-27, 29-31, 33, and 34 of Application Serial Number 10/671,086 under 35 U.S.C. § 112, first paragraph:

11. Claims 7, 8, 22-27, 29-31, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The definitions, meets and bounds of the term developed flow and what Reynolds number indicates a turbulent flow, critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See In re Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Clearly the rate of transfer of heat depends upon such limitations and applicant's alleged invention will not operate as claimed without such.

Paper Number 20050411, Application Serial No. 10/671,086, at 6-7.

14. The statement from the Examiner quoted in the paragraph above is incorrect, in view of the state of the art as of the filing date of Application Serial Number 10/671,086 and the knowledge possessed by one skilled in the art at the time of filing of the application. The Examiner's assertions are not correct, for the following reasons:

15. One of ordinary skill in the art of target assemblies for producing fluorine-18 understands the meaning of developed flow and turbulent flow. Further, such a person understands how to design a conduit in order to obtain a developed flow, and such a person understands what Reynolds number indicates a turbulent flow. In order to design such a conduit, it is necessary to have information on the conduit diameter, the mass velocity, the viscosity and density of the fluid, and other factors. The determination and consideration of these factors is within the ability of one of ordinary skill in the art. Accordingly, a reading of Application Serial Number 10/671,086, along with the knowledge and skill one skilled in the art would have, provides sufficient information for one of ordinary skill in the art to understand developed flow and what Reynolds number indicates a turbulent flow.

**Examiner's Statement Regarding Rejection of Claims 10 and 32 under 35 U.S.C. § 112, first paragraph**

16. I have reviewed the U.S. Patent and Trademark Office Action, Paper Number 20050411, which contains the following statement on page 7 with respect to the Examiners rejection of Claims 10 and 32 of Application Serial Number 10/671,086 under 35 U.S.C. § 112, first paragraph:

12. Claims 10 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for irradiation by a proton particle beam, does not reasonably provide enablement for irradiation by any other type of particle beam. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The limitations "irradiation" and "bombarded with a particle beam" includes the use of other types of particles other than protons. The disclosure fails to define exactly what or which "particles" applicant's invention is capable of use with. Would the target still function if for example it was bombarded or irradiated with a beam of gamma, Helium, neutron or electron particles?

17. The statement from the Examiner quoted in the paragraph above is incorrect, in view of the state of the art as of the filing date of Application Serial Number 10/671,086 and the knowledge possessed by one skilled in the art at the time of filing of the application. The Examiner's assertions are not correct, for the following reasons:

18. One of ordinary skill in the art of target assemblies for producing fluorine-18 understands particle beams as disclosed in Application Serial Number 10/671,086. The target assemblies discussed in the Application have a very specific use, namely, to produce fluorine-18 through particle beam bombardment of oxygen-18 enriched water. Additionally, the production of fluorine-18 requires much associated equipment in addition to the target assembly. One skilled in the art of target assemblies for producing radioactive isotopes understands how the particle beams are generated and applied to the target assembly. One skilled in the art understands the atomic reactions occurring in the target chamber and the volumetric heat loads developed based on the bombarding particles, the beam energy and current, and the target material.

19. I have reviewed the specification of Application Serial Number 10/671,086 and the claims therein, including Claims 10 and 32. I find the disclosure to clearly and completely describe the environment in which the target assemblies operate. Ignoring the atomic reactions of the isotopes as a result of the particle beam, the particle beam is a heat source. My understanding of the claims is that the invention relates to the removal of the heat caused by the particle beam. The specifics of the particle beam other than its heating capabilities is not relevant to the invention, as I understand it. Accordingly, a reading of Application Serial Number 10/671,086, along with the knowledge one skilled in the art would have, provides sufficient information for one of ordinary skill in the art to make and use the target assembly as described in Claims 10 and 32 without undue experimentation.

**Examiner's Statement Regarding Rejection of Claim 29 under 35 U.S.C. § 112, first paragraph**

20. I have reviewed the U.S. Patent and Trademark Office Action, Paper Number 20050411, which contains the following statement on page 7 with respect to the Examiners rejection of Claim 29 of Application Serial Number 10/671,086 under 35 U.S.C. § 112, first paragraph:

13. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The required size of the cooling channel, critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. *See In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The disclosure fails to disclose the basis for, how and in what manner the cooling channels are sized in order to sustain or even develop a developed flow within. It is questioned how and in what manner the applicant has determined the type of flow (laminar, turbulent, etc.) within ANY of the cooling channels.

21. The statement from the Examiner quoted in the paragraph above is incorrect, in view of the state of the art as of the filing date of Application Serial Number 10/671,086 and the knowledge possessed by one skilled in the art at the time of filing of the application. The Examiner's assertions are not correct, for the following reasons:

22. As stated previously, one skilled in the art is familiar with fluid dynamics and flow in conduits. For example, it is not uncommon for an engineer to size a conduit for developed flow, based on the fluid characteristics flowing through that conduit and the available pressure and volume of the fluid. Standard formulas and tables are available for determining the diameter and length of conduits in order to have laminar flow, developed turbulent flow, or variations thereof. Likewise determining the type of flow within a conduit is a basic skill possessed by one with skill in the art. Accordingly, one skilled in the art has the ability to perform basic fluid dynamic calculations to determine the type of flow within a conduit such as the cooling channels. Further, one skilled in the art has the ability to size a conduit in order to achieve a specific type of flow within that conduit.

**Examiner's Statement Regarding Rejection of Claims 8, 25-27, and 34 for being indefinite**

23. I have reviewed the U.S. Patent and Trademark Office Action, Paper Number 20050411, which contains the following statement on page 8 with respect to the Examiners rejection of Claims 8, 25-27, and 34 of Application Serial Number 10/671,086 for being indefinite:

15. The phrase "Reynolds number indicating a turbulent flow" in Claims 8, 25-27 and 34 is a relative term which renders the claims indefinite. The phrase "Reynolds number indicating a turbulent flow " is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The requisite degree of how or what numbers would satisfy said claims is unascertainable.

24. The statement from the Examiner quoted in the paragraph above is incorrect, in view of the state of the art as of the filing date of Application Serial Number 10/671,086 and the knowledge possessed by one skilled in the art at the time of filing of the application. The Examiner's assertions are not correct, for the following reasons:

25. Engineering students typically learn about the Reynolds number in their first fluid dynamics course. It is commonly known in the art that the Reynolds number is



calculated by the equation:  $Re = v_s \rho L / \mu$  where  $v_s$  is the mean fluid velocity,  $\rho$  is the fluid density,  $L$  is the characteristic length, and  $\mu$  is the absolute dynamic fluid viscosity. The Reynolds number is the ratio of inertial forces ( $v_s \rho$ ) to viscous forces ( $\mu/L$ ) and is used for determining whether a flow will be laminar or turbulent. The transition between laminar and turbulent flow is often indicated by a critical Reynolds number, which depends on the exact flow configuration and is determined experimentally. However, within circular pipes the critical Reynolds number is generally accepted to be 2300, where the Reynolds number is based on the pipe diameter and the mean velocity  $v_s$  within the pipe. But typically, any pipe configuration that falls within the range of Reynolds numbers from about 2000 to 4000 is avoided to ensure that the flow is either laminar or turbulent.

26. One skilled in the art of the target assemblies is familiar with the Reynolds number as described in the paragraph above. Accordingly, the statement "Reynolds number indicating a turbulent flow " is a precise statement to one skilled in the art and readily conveys to one skilled in the art the information necessary to apply the limitation.

**Examiner's Statement Regarding Rejection of Claim 20**

27. I have reviewed the U.S. Patent and Trademark Office Action, Paper Number 20050411, which contains the following statement on page 9 with respect to the Examiners rejection of Claim 20 of Application Serial Number 10/671,086:

17. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are:

A. The manner of shaping a target chamber such that a steam jet is formed in the manner proposed,

B. the manner of shaping a target chamber such that a steam jet flows into a steam bubble in the manner proposed,

**Declaration of Charles W. Alvord**

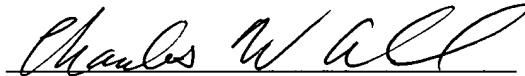
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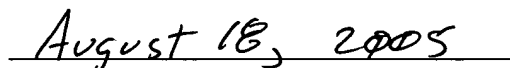
C. the manner in which the first cooling channel transfers heat directly from the steam bubble thereby condensing said bubble when the first cooling channel is isolated from the target chamber and therefore said steam bubble.

28. The statement from the Examiner quoted in the paragraph above is incorrect, in view of the disclosure contained within Application Serial Number 10/671,086, the state of the art as of the filing date of Application Serial Number 10/671,086, and the knowledge possessed by one skilled in the art at the time of filing of the application. The Examiner's assertions are not correct, for the following reasons:

29. I have reviewed Application Serial Number 10/671,086 in view of the Examiner's comments stated above. The Application describes the jet in the target chamber in paragraphs 24 and 28. As stated previously, one skilled in the art at the time of filing the Application is familiar with fluid dynamics, particularly as fluid dynamics relates to the fluid within the target chamber. Application Serial Number 10/671,086 includes a discussion of the target chamber configuration and the steam jet. See, for example, paragraphs 24 and 28-30 in the Application. Accordingly, a reading of Application Serial Number 10/671,086, along with the knowledge and skill one skilled in the art would have, provides sufficient information for one of ordinary skill in the art to understand, make, and use the invention as described in Claim 20.

Respectfully submitted,

  
Charles W. Alvord

  
Date